

Check whether specific cisplatin-associated genes (from the literature) predict response in our cohort

November 17, 2008

1 Getting started

```
> options(width = 70)
```

1.1 Load add-on packages

```
> library(affy)
> library(gdata)
> library(genefilter)
> library(hgu133plus2.db)
```

1.2 Load the RMA-processed expression values

```
> load("/home/projects/sbge_cancer/data/exprs/platinum.rma.RData")
```

1.3 Load the table of cisplatin-associated probe sets

```
> assocTable <- read.xls("aron/chb/projects/richardson/platinum/genes assoc with cisplat.
+   as.is = TRUE)
```

Converting xls file to csv file... Done.

Reading csv file... Done.

```
> str(assocTable)
```

```
'data.frame':      115 obs. of  2 variables:
 $ Gene.Name: chr  "ABL1" "AKT1" "adenosylmethionine decarboxylase 1" "baculoviral IAP rep
 $ Gene.ID   : num  25 207 262 330 331 332 356 374 468 472 ...
```

1.4 Remove outliers and non-cisplatin-treated samples

```
> ok.sample <- !is.na(platinum.rma$Miller)
> ok.sample[platinum.rma$Chip %in% c("P9", "P20")] <- FALSE
> plat.rma <- platinum.rma[, ok.sample]
```

1.5 Define the response groups

We are interested in the Miller-Payne grade. We are also interested in the distinction between two response groups: Miller-Payne grades 0-2, and M-P grades 3-5.

```
> grade <- plat.rma$Miller.Payne.Grade  
> response <- factor(ifelse(grade > 2, "MP345", "MP012"))  
> table(response = response, MP.grade = grade)  
  
MP.grade  
response 0 1 2 3 4 5  
MP012 3 5 4 0 0 0  
MP345 0 0 0 4 4 4
```

1.6 Miscellaneous

Get gene symbol, name and Entrez ID for each probe set:

```
> symb <- sapply(mget(featureNames(plat.rma), hgu133plus2SYMBOL),  
+     function(x) x[1])  
> gene <- sapply(mget(featureNames(plat.rma), hgu133plus2GENENAME),  
+     function(x) x[1])  
> entrezID <- sapply(mget(featureNames(plat.rma), hgu133plus2ENTREZID),  
+     function(x) x[1])
```

A convenient plotting function:

```
> pl <- function(x, main) {  
+   par(mfrow = c(3, 5), mar = c(5, 4, 1, 2), oma = c(0,  
+     0, 2, 0))  
+   layout(matrix(1:2, nrow = 1), widths = c(1, 2))  
+   p <- t.test(x ~ response)$p.value  
+   p.txt <- paste("P =", format(p, digits = 2, scientific = FALSE))  
+   corr <- cor.test(x, grade)  
+   corr.txt <- paste("cor =", format(corr$estimate,  
+     digits = 2, scientific = FALSE), "; p =", format(corr$p.value,  
+     digits = 2, scientific = FALSE))  
+   ylim <- range(x)  
+   ylim <- c(ylim[1], ylim[2] + (diff(ylim) * 0.1))  
+   boxplot(x ~ response, ylim = ylim)  
+   legend("top", legend = p.txt, bty = "n")  
+   stripchart(x ~ grade, ylim = ylim, method = "jitter",  
+     vertical = TRUE, xlab = "MP grade", ylab = "")  
+   legend("top", legend = corr.txt, bty = "n")  
+   title(outer = TRUE, main = main)  
+ }
```

1.7 Map the cisplatin-associated genes to probe sets

```
> cis.probes <- names(entrezID)[entrezID %in% as.character(assocTable$Gene.ID)]  
> str(cis.probes)  
  
chr [1:360] "1552263_at" "1552264_a_at" "1553244_at" ...
```

2 Evaluation of genes by t test

Create a subset of the gene expression matrix corresponding to the cisplatin-associated genes.

```
> plat.rma.sub <- plat.rma[cis.probes, ]
```

Perform t tests on each probe set.

```
> ttests <- rowttests(plat.rma.sub, fac = response)
```

Put data for each probe set together.

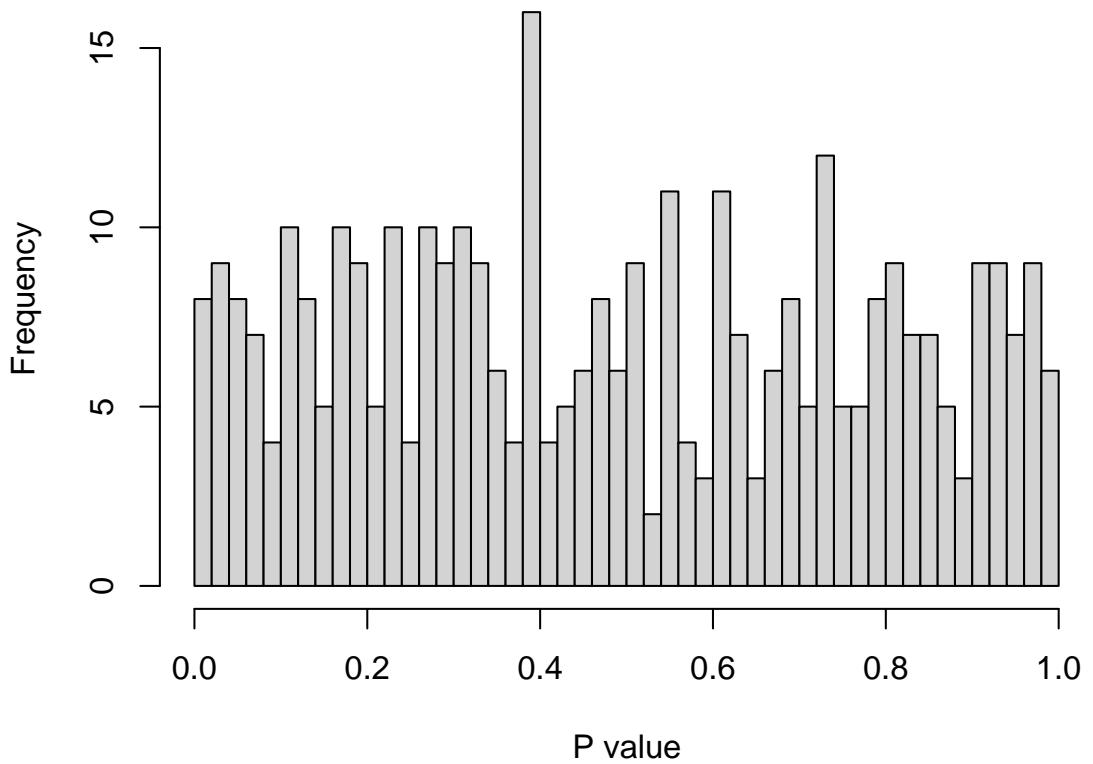
```
> d <- data.frame(symbol = symb[cis.probes], gene = gene[cis.probes],
+   entrez = entrezID[cis.probes], dm = ttests$dm, p.val = ttests$p.value,
+   stringsAsFactors = FALSE)
> d$sig <- c("***", "**", "*", ".", "")[cut(d$p.val, breaks = c(-1,
+   0.001, 0.01, 0.05, 0.1, 2))]
> too.long <- nchar(d$gene) > 20
> d$gene[too.long] <- paste(substr(d$gene[too.long], 1,
+   17), "...", sep = "")
```

2.1 Distribution of P values

These are the UNCORRECTED P values.

```
> hist(d$p.val, n = 40, col = "lightgray", xlab = "P value",
+   main = "t test, MP-0,1,2 vs. MP-3,4,5")
```

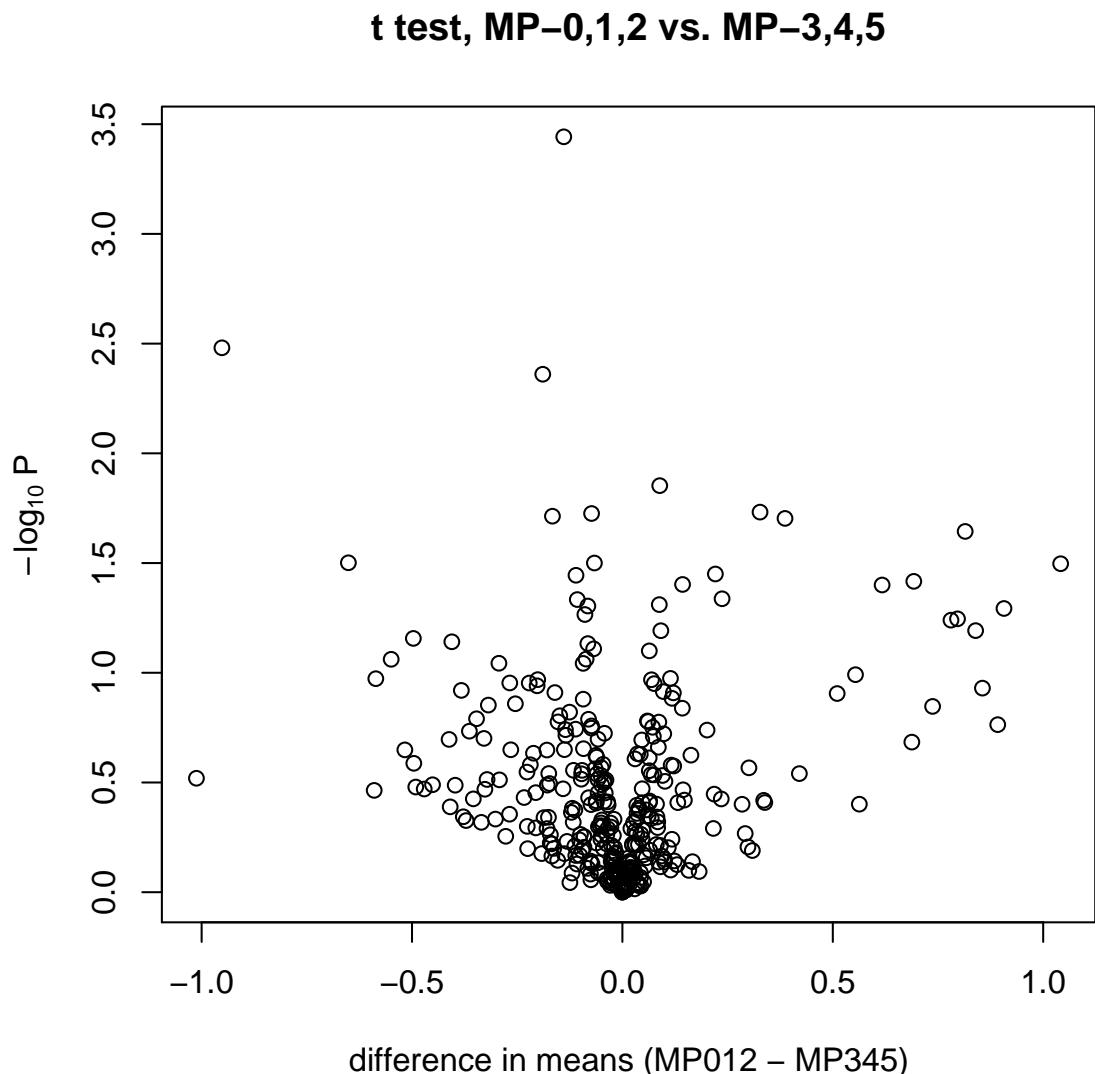
t test, MP–0,1,2 vs. MP–3,4,5



2.2 Volcano plot

These are the UNCORRECTED P values.

```
> plot(x = d$dm, y = -log10(d$p.val), xlab = "difference in means (MP012 - MP345)",  
+       ylab = expression(paste(-log[10], " P")), main = "t test, MP-0,1,2 vs. MP-3,4,5")
```



2.3 Correct P values for multiple hypotheses

How many hypotheses (genes) do we have?

```
> nh <- length(unique(d$symbol))
```

```
> nh
```

```
[1] 114
```

```
> d$corrected <- d$p.val * nh
```

2.4 List some possibly interesting results

```
> interesting <- d$p.val < 0.05
```

```
> options(width = 90)
```

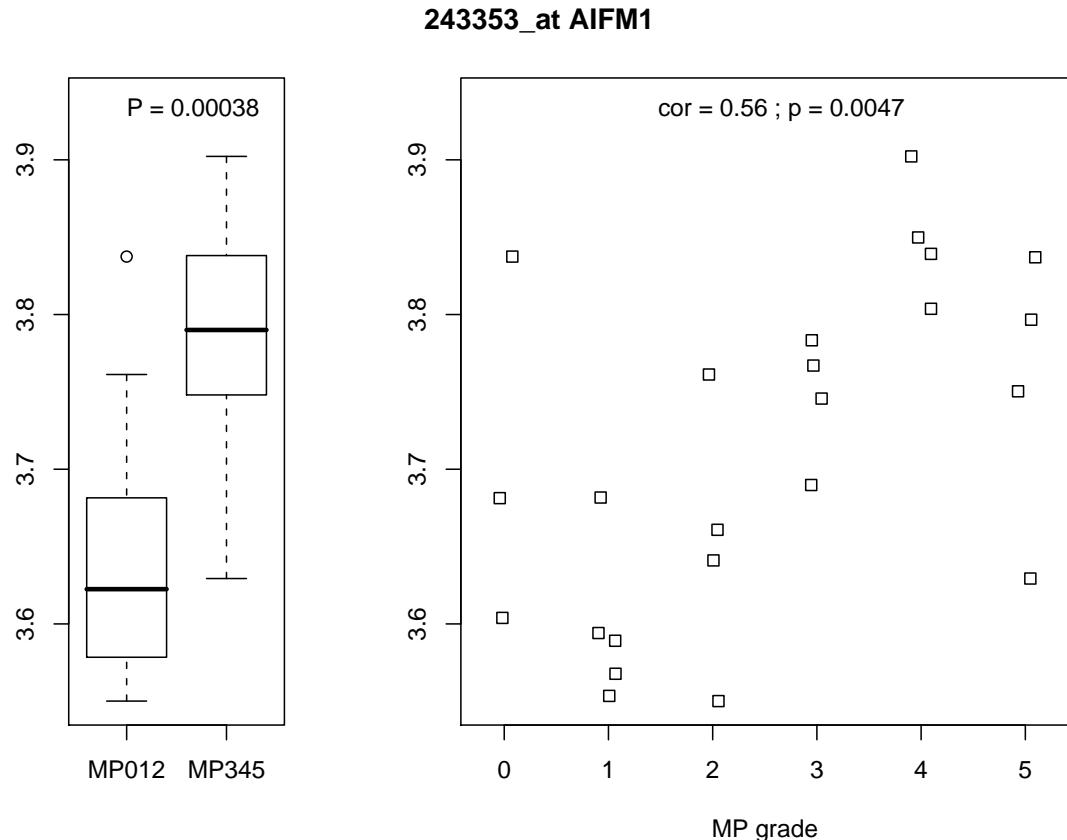
```
> print(d[interesting, ], digits = 2)
```

	symbol	gene	entrez	dm	p.val	sig	corrected
1552264_a_at	MAPK1 mitogen-activated...		5594	0.386	0.01979	*	2.256
1560395_at	CD24 CD24 molecule		934	-0.073	0.01880	*	2.143
1566484_at	FHIT fragile histidine...		2272	0.143	0.03957	*	4.512
202095_s_at	BIRC5 baculoviral IAP r...		332	-0.952	0.00330	**	0.377
203971_at	SLC31A1 solute carrier fa...		1317	-0.651	0.03152	*	3.593
204490_s_at	CD44 CD44 molecule (In...		960	0.617	0.03980	*	4.537
206155_at	ABCC2 ATP-binding casse...		1244	0.221	0.03546	*	4.042
208651_x_at	CD24 CD24 molecule		934	1.042	0.03183	*	3.629
208992_s_at	STAT3 signal transducer...		6774	0.327	0.01853	*	2.112
209835_x_at	CD44 CD44 molecule (In...		960	0.815	0.02269	*	2.586
209960_at	HGF hepatocyte growth...		3082	-0.166	0.01933	*	2.204
210334_x_at	BIRC5 baculoviral IAP r...		332	-0.189	0.00436	**	0.497
210998_s_at	HGF hepatocyte growth...		3082	0.089	0.01403	*	1.600
212014_x_at	CD44 CD44 molecule (In...		960	0.693	0.03830	*	4.367
214258_x_at	HTATIP HIV-1 Tat interac...		10524	0.237	0.04599	*	5.243
214727_at	BRCA2 breast cancer 2, ...		675	-0.082	0.04963	*	5.657
237938_at	EGFR epidermal growth ...		1956	0.088	0.04890	*	5.574
240964_at	PTEN phosphatase and t...		5728	-0.107	0.04638	*	5.287
242622_x_at	PTEN phosphatase and t...		5728	-0.067	0.03160	*	3.602
243026_x_at	XIAP X-linked inhibito...		331	-0.110	0.03594	*	4.098
243353_at	AIFM1 apoptosis-inducin...		9131	-0.139	0.00036	***	0.041

```
> options(width = 70)
```

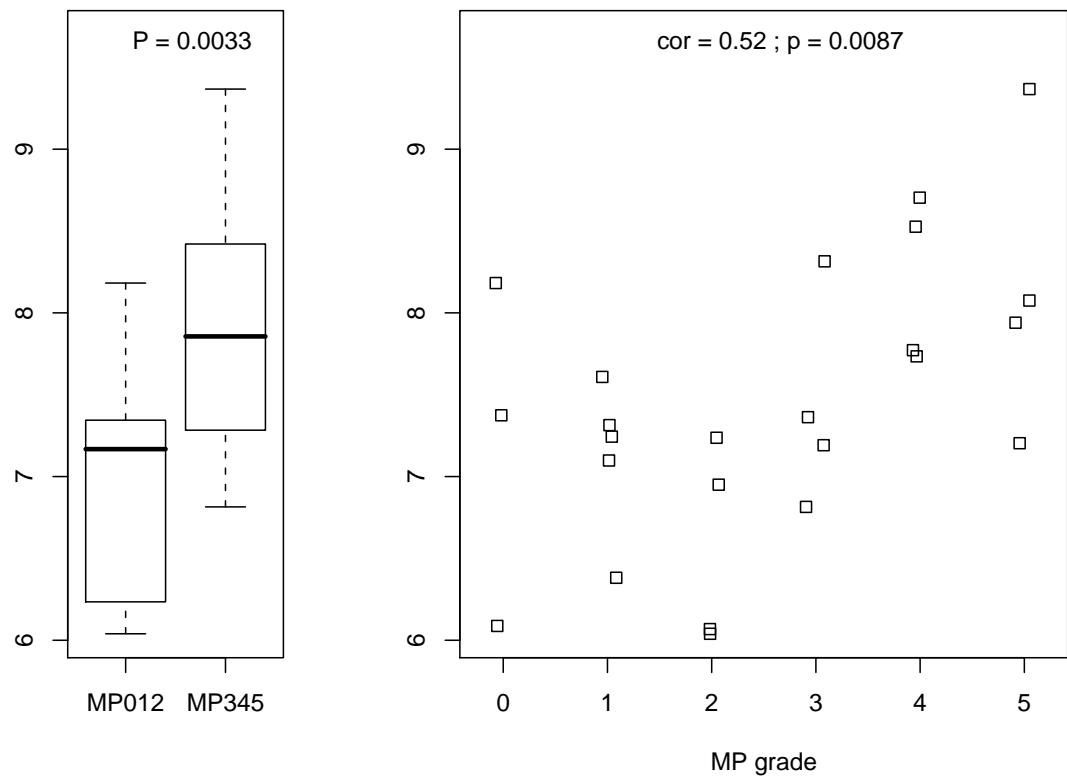
2.5 Visualize the most statistically significant probe sets

```
> pr <- "243353_at"  
> pl(exprs(plat.rma)[pr, ], main = paste(pr, symb[pr]))
```



```
> pr <- "202095_s_at"  
> pl(exprs(plat.rma)[pr, ], main = paste(pr, symb[pr]))
```

202095_s_at BIRC5



2.6 List of all results

```
> options(width = 90)
> print(d[order(d$symbol), ], digits = 2)
```

	symbol	gene	entrez	dm	p.val	sig	corrected
209993_at	ABCB1 ATP-binding casse...	5243	0.03113	0.60954			69.488
209994_s_at	ABCB1 ATP-binding casse...	5243	-0.09586	0.64539			73.575
243951_at	ABCB1 ATP-binding casse...	5243	0.04708	0.33758			38.484
206155_at	ABCC2 ATP-binding casse...	1244	0.22093	0.03546	*		4.042
1554918_a_at	ABCC4 ATP-binding casse...	10257	0.06363	0.24418			27.837
1555039_a_at	ABCC4 ATP-binding casse...	10257	-0.00214	0.96854			110.413
203196_at	ABCC4 ATP-binding casse...	10257	-0.51701	0.22453			25.597
243928_s_at	ABCC4 ATP-binding casse...	10257	-0.15301	0.16738			19.081
244053_at	ABCC4 ATP-binding casse...	10257	-0.07327	0.17467			19.912
202123_s_at	ABL1 c-abl oncogene 1,...	25	-0.17940	0.22491			25.640
205512_s_at	AIFM1 apoptosis-inducin...	9131	0.04328	0.85588			97.570
243353_at	AIFM1 apoptosis-inducin...	9131	-0.13935	0.00036	***		0.041
207163_s_at	AKT1 v-akt murine thym...	207	0.04826	0.52104			59.398
201196_s_at	AMD1 adenosylmethionin...	262	0.33577	0.38130			43.468
201197_at	AMD1 adenosylmethionin...	262	-0.08227	0.77843			88.741
205239_at	AREG amphiregulin (sch...	374	-0.37803	0.45305			51.647
215564_at	AREG amphiregulin (sch...	374	-0.00094	0.97786			111.476
200779_at	ATF4 activating transcr...	468	0.10022	0.72898			83.103
204998_s_at	ATF5 activating transcr...	22809	0.08219	0.45437			51.798
204999_s_at	ATF5 activating transcr...	22809	0.07547	0.11201			12.769
217389_s_at	ATF5 activating transcr...	22809	0.02961	0.60309			68.753
230938_x_at	ATF5 activating transcr...	22809	0.02301	0.73568			83.868
1553387_at	ATM ataxia telangiect...	472	-0.08050	0.16287			18.567
1554631_at	ATM ataxia telangiect...	472	-0.02799	0.48363			55.134
1570352_at	ATM ataxia telangiect...	472	-0.01995	0.46502			53.012
208442_s_at	ATM ataxia telangiect...	472	0.03426	0.54159			61.742
210858_x_at	ATM ataxia telangiect...	472	-0.07224	0.74071			84.441
212672_at	ATM ataxia telangiect...	472	0.09024	0.76596			87.319
240621_at	ATM ataxia telangiect...	472	0.01610	0.72378			82.511
209902_at	ATR ataxia telangiect...	545	-0.02272	0.91497			104.307
209903_s_at	ATR ataxia telangiect...	545	-0.05771	0.81289			92.669
233288_at	ATR ataxia telangiect...	545	0.00075	0.98167			111.910
202387_at	BAG1 BCL2-associated a...	573	0.03639	0.90524			103.197
211475_s_at	BAG1 BCL2-associated a...	573	0.02698	0.85831			97.847
229720_at	BAG1 BCL2-associated a...	573	-0.02856	0.93030			106.054
203728_at	BAK1 BCL2-antagonist/k...	578	-0.04984	0.54933			62.623
205345_at	BARD1 BRCA1 associated ...	580	-0.17112	0.54711			62.370
208478_s_at	BAX BCL2-associated X...	581	-0.02529	0.68415			77.993
211833_s_at	BAX BCL2-associated X...	581	0.01081	0.85932			97.963
203684_s_at	BCL2 B-cell CLL/lympho...	596	-0.05108	0.57373			65.405
203685_at	BCL2 B-cell CLL/lympho...	596	-0.58601	0.10637			12.126
207004_at	BCL2 B-cell CLL/lympho...	596	-0.02589	0.61125			69.683

207005_s_at	BCL2	B-cell CLL/lympho...	596	-0.04285	0.31129		35.487
232210_at	BCL2	B-cell CLL/lympho...	596	-0.39730	0.32530		37.084
232614_at	BCL2	B-cell CLL/lympho...	596	-0.25435	0.13836		15.773
237837_at	BCL2	B-cell CLL/lympho...	596	-0.00898	0.83541		95.237
244035_at	BCL2	B-cell CLL/lympho...	596	-0.09325	0.09059	.	10.327
1569067_at	BCL2L1	BCL2-like 1	598	0.02641	0.78421		89.400
206665_s_at	BCL2L1	BCL2-like 1	598	0.06833	0.29105		33.179
212312_at	BCL2L1	BCL2-like 1	598	-0.16042	0.12305		14.027
215037_s_at	BCL2L1	BCL2-like 1	598	-0.01933	0.68957		78.612
231228_at	BCL2L1	BCL2-like 1	598	0.04386	0.54418		62.036
1561652_at	BECN1	beclin 1, autophag...	8678	-0.01909	0.62600		71.364
208945_s_at	BECN1	beclin 1, autophag...	8678	-0.05064	0.48327		55.093
208946_s_at	BECN1	beclin 1, autophag...	8678	0.08585	0.72895		83.100
204493_at	BID	BH3 interacting dom...	637	-0.16308	0.63122		71.959
211725_s_at	BID	BH3 interacting dom...	637	-0.00044	0.99903		113.889
227143_s_at	BID	BH3 interacting dom...	637	-0.29223	0.30758		35.065
210538_s_at	BIRC3	baculoviral IAP r...	330	-0.11967	0.81817		93.271
230499_at	BIRC3	baculoviral IAP r...	330	0.13167	0.39060		44.528
1555826_at	BIRC5	baculoviral IAP r...	332	-0.29346	0.09048	.	10.315
202094_at	BIRC5	baculoviral IAP r...	332	-0.22671	0.28342		32.310
202095_s_at	BIRC5	baculoviral IAP r...	332	-0.95172	0.00330	**	0.377
210334_x_at	BIRC5	baculoviral IAP r...	332	-0.18922	0.00436	**	0.497
204531_s_at	BRCA1	breast cancer 1, BRCA1	672	0.55398	0.10200		11.628
211851_x_at	BRCA1	breast cancer 1, BRCA1	672	0.07163	0.17715		20.195
208368_s_at	BRCA2	breast cancer 2, BRCA2	675	-0.03469	0.51359		58.549
214727_at	BRCA2	breast cancer 2, BRCA2	675	-0.08210	0.04963	*	5.657
1554479_a_at	CARD8	caspase recruitment d...	22900	-0.30171	0.46421		52.920
204950_at	CARD8	caspase recruitment d...	22900	-0.21133	0.23254		26.510
228641_at	CARD8	caspase recruitment d...	22900	-0.01178	0.93753		106.878
232969_at	CARD8	caspase recruitment d...	22900	-0.05780	0.20081		22.893
202763_at	CASP3	caspase 3, apoptosis	836	-0.07565	0.72091		82.184
236729_at	CASP3	caspase 3, apoptosis	836	0.01568	0.73747		84.071
203984_s_at	CASP9	caspase 9, apoptosis	842	-0.20272	0.11463		13.068
210775_x_at	CASP9	caspase 9, apoptosis	842	-0.08910	0.05426	.	6.185
1562028_at	CCND3	cyclin D3	896	-0.06827	0.07776	.	8.865
201700_at	CCND3	cyclin D3	896	-0.05782	0.73301		83.563
1560395_at	CD24	CD24 molecule	934	-0.07327	0.01880	*	2.143
208650_s_at	CD24	CD24 molecule	934	0.89198	0.17234		19.647
208651_x_at	CD24	CD24 molecule	934	1.04154	0.03183	*	3.629
209771_x_at	CD24	CD24 molecule	934	0.78088	0.05756	.	6.562
209772_s_at	CD24	CD24 molecule	934	0.85562	0.11748		13.393
216379_x_at	CD24	CD24 molecule	934	0.79639	0.05678	.	6.473
266_s_at	CD24	CD24 molecule	934	0.83942	0.06424	.	7.324
1557905_s_at	CD44	CD44 molecule (Intron)	960	0.90682	0.05092	.	5.805
1565868_at	CD44	CD44 molecule (Intron)	960	-0.14100	0.33778		38.506
204489_s_at	CD44	CD44 molecule (Intron)	960	0.33841	0.39010		44.471
204490_s_at	CD44	CD44 molecule (Intron)	960	0.61716	0.03980	*	4.537

209835_x_at	CD44	CD44 molecule (In...	960	0.81458	0.02269	*	2.586
210916_s_at	CD44	CD44 molecule (In...	960	0.12191	0.26592		30.314
212014_x_at	CD44	CD44 molecule (In...	960	0.69253	0.03830	*	4.367
212063_at	CD44	CD44 molecule (In...	960	0.51038	0.12430		14.170
216056_at	CD44	CD44 molecule (In...	960	0.02401	0.61164		69.727
216062_at	CD44	CD44 molecule (In...	960	0.14238	0.14501		16.531
217523_at	CD44	CD44 molecule (In...	960	-0.10124	0.67958		77.473
229221_at	CD44	CD44 molecule (In...	960	0.21615	0.51217		58.387
234411_x_at	CD44	CD44 molecule (In...	960	-0.01275	0.80331		91.577
234418_x_at	CD44	CD44 molecule (In...	960	0.11420	0.10605		12.090
201130_s_at	CDH1	cadherin 1, type ...	999	0.06395	0.07946	.	9.059
201131_s_at	CDH1	cadherin 1, type ...	999	-0.37145	0.47136		53.735
207039_at	CDKN2A	cyclin-dependent ...	1029	-0.12476	0.90400		103.056
209644_x_at	CDKN2A	cyclin-dependent ...	1029	0.05024	0.89622		102.169
211156_at	CDKN2A	cyclin-dependent ...	1029	0.14410	0.34130		38.908
208485_x_at	CFLAR	CASP8 and FADD-li...	8837	-0.01532	0.78255		89.211
209508_x_at	CFLAR	CASP8 and FADD-li...	8837	0.08540	0.21847		24.905
209939_x_at	CFLAR	CASP8 and FADD-li...	8837	-0.16757	0.68403		77.979
210563_x_at	CFLAR	CASP8 and FADD-li...	8837	-0.15375	0.71556		81.574
210564_x_at	CFLAR	CASP8 and FADD-li...	8837	0.04289	0.81441		92.843
211316_x_at	CFLAR	CASP8 and FADD-li...	8837	-0.17314	0.31968		36.443
211317_s_at	CFLAR	CASP8 and FADD-li...	8837	0.01153	0.79250		90.345
211862_x_at	CFLAR	CASP8 and FADD-li...	8837	0.01009	0.82487		94.035
214486_x_at	CFLAR	CASP8 and FADD-li...	8837	0.00348	0.97612		111.278
214618_at	CFLAR	CASP8 and FADD-li...	8837	0.04718	0.39078		44.549
217654_at	CFLAR	CASP8 and FADD-li...	8837	0.03481	0.43724		49.845
237367_x_at	CFLAR	CASP8 and FADD-li...	8837	-0.02078	0.82249		93.764
239629_at	CFLAR	CASP8 and FADD-li...	8837	-0.54952	0.08679	.	9.894
210416_s_at	CHEK2	CHK2 checkpoint h...	11200	-0.01949	0.87424		99.664
203953_s_at	CLDN3	claudin 3	1365	0.03954	0.41359		47.149
203954_x_at	CLDN3	claudin 3	1365	0.08398	0.47773		54.461
1569421_at	CLDN4	claudin 4	1364	0.07351	0.19486		22.214
201428_at	CLDN4	claudin 4	1364	0.11781	0.57359		65.389
202790_at	CLDN7	claudin 7	1366	0.16287	0.23731		27.054
223020_at	CLPTM1L	CLPTM1-like	81037	0.29180	0.54012		61.574
226935_s_at	CLPTM1L	CLPTM1-like	81037	0.05407	0.75938		86.569
229416_at	CLPTM1L	CLPTM1-like	81037	0.03001	0.24689		28.145
203804_s_at	CROP	cisplatin resist...	51747	-0.32677	0.33941		38.693
208835_s_at	CROP	cisplatin resist...	51747	-0.45123	0.32373		36.906
220044_x_at	CROP	cisplatin resist...	51747	-0.22607	0.50097		57.110
229193_at	CROP	cisplatin resist...	51747	-0.01750	0.75182		85.708
241086_at	CROP	cisplatin resist...	51747	0.00035	0.99035		112.900
241792_x_at	CROP	cisplatin resist...	51747	-0.17913	0.51287		58.467
242389_at	CROP	cisplatin resist...	51747	-0.03457	0.88732		101.154
209283_at	CRYAB	crystallin, alpha B	1410	0.15770	0.79528		90.662
201041_s_at	DUSP1	dual specificity ...	1843	0.42058	0.28799		32.831
201044_x_at	DUSP1	dual specificity ...	1843	0.09141	0.06430	.	7.330

226578_s_at	DUSP1 dual specificity ...	1843	0.05694	0.42159	48.061	
1565483_at	EGFR epidermal growth ...	1956	0.56306	0.39703	45.262	
1565484_x_at	EGFR epidermal growth ...	1956	0.68783	0.20696	23.594	
201983_s_at	EGFR epidermal growth ...	1956	0.14732	0.38034	43.359	
201984_s_at	EGFR epidermal growth ...	1956	0.09066	0.61232	69.805	
210984_x_at	EGFR epidermal growth ...	1956	0.05031	0.67566	77.025	
211550_at	EGFR epidermal growth ...	1956	-0.00217	0.96842	110.400	
211551_at	EGFR epidermal growth ...	1956	0.02644	0.48270	55.028	
211607_x_at	EGFR epidermal growth ...	1956	0.02468	0.77284	88.104	
224999_at	EGFR epidermal growth ...	1956	0.03033	0.81859	93.320	
232120_at	EGFR epidermal growth ...	1956	-0.05044	0.27036	30.821	
232541_at	EGFR epidermal growth ...	1956	-0.49108	0.33156	37.798	
232925_at	EGFR epidermal growth ...	1956	0.07529	0.29189	33.276	
233044_at	EGFR epidermal growth ...	1956	-0.09118	0.55746	63.551	
237938_at	EGFR epidermal growth ...	1956	0.08767	0.04890	*	5.574
243327_at	EGFR epidermal growth ...	1956	-0.04268	0.18866	21.507	
203719_at	ERCC1 excision repair c...	2067	0.03403	0.90908	103.635	
203720_s_at	ERCC1 excision repair c...	2067	0.00847	0.97003	110.584	
228131_at	ERCC1 excision repair c...	2067	-0.49680	0.06970	.	7.946
213468_at	ERCC2 excision repair c...	2068	-0.01241	0.85559	97.537	
202176_at	ERCC3 excision repair c...	2071	0.01605	0.92524	105.478	
210158_at	ERCC4 excision repair c...	2072	0.03805	0.60719	69.220	
235215_at	ERCC4 excision repair c...	2072	-0.26520	0.22426	25.566	
202414_at	ERCC5 excision repair c...	2073	0.23492	0.37575	42.836	
233415_at	ERCC5 excision repair c...	2073	-0.04609	0.26124	29.781	
207347_at	ERCC6 excision repair c...	2074	0.09737	0.12181	13.887	
204363_at	F3 coagulation facto...	2152	0.21812	0.35712	40.711	
203805_s_at	FANCA Fanconi anemia, c...	2175	-0.13425	0.19268	21.966	
203806_s_at	FANCA Fanconi anemia, c...	2175	-0.22140	0.11137	12.696	
215530_at	FANCA Fanconi anemia, c...	2175	-0.05115	0.29340	33.448	
236976_at	FANCA Fanconi anemia, c...	2175	-0.13535	0.18163	20.706	
1553244_at	FANCB Fanconi anemia, c...	2187	-0.06473	0.27391	31.226	
1557217_a_at	FANCB Fanconi anemia, c...	2187	0.02014	0.51240	58.413	
1557218_s_at	FANCB Fanconi anemia, c...	2187	-0.03499	0.38772	44.200	
243597_at	FANCB Fanconi anemia, c...	2187	-0.02140	0.55098	62.812	
1559513_a_at	FANCC Fanconi anemia, c...	2176	-0.02433	0.70632	80.521	
205189_s_at	FANCC Fanconi anemia, c...	2176	-0.02667	0.84821	96.695	
242654_at	FANCC Fanconi anemia, c...	2176	-0.01739	0.66783	76.132	
243637_at	FANCC Fanconi anemia, c...	2176	-0.05838	0.30582	34.863	
1568889_at	FANCD2 Fanconi anemia, c...	2177	-0.06079	0.28973	33.029	
1568891_x_at	FANCD2 Fanconi anemia, c...	2177	-0.08215	0.07360	.	8.390
223545_at	FANCD2 Fanconi anemia, c...	2177	-0.01570	0.79484	90.611	
242560_at	FANCD2 Fanconi anemia, c...	2177	-0.19189	0.66674	76.009	
220255_at	FANCE Fanconi anemia, c...	2178	-0.09153	0.55951	63.785	
1556713_at	FANCF Fanconi anemia, c...	2188	0.01448	0.69789	79.559	
218689_at	FANCF Fanconi anemia, c...	2188	-0.38279	0.12028	13.712	
222713_s_at	FANCF Fanconi anemia, c...	2188	-0.14879	0.15699	17.896	

228688_at	FANCF	Fanconi anemia, c...	2188	-0.04537	0.63037	71.862
203564_at	FANCG	Fanconi anemia, c...	2189	-0.13156	0.58650	66.861
210865_at	FASLG	Fas ligand (TNF s...	356	-0.00032	0.99797	113.768
211333_s_at	FASLG	Fas ligand (TNF s...	356	-0.04379	0.38556	43.954
1566484_at	FHIT	fragile histidine...	2272	0.14297	0.03957	*
1566485_at	FHIT	fragile histidine...	2272	0.04607	0.20236	23.068
206492_at	FHIT	fragile histidine...	2272	0.08105	0.39677	45.231
202288_at	FRAP1	FK506 binding pro...	2475	-0.11890	0.41427	47.227
215381_at	FRAP1	FK506 binding pro...	2475	0.01791	0.77065	87.854
203925_at	GCLM	glutamate-cystein...	2730	0.16656	0.72545	82.701
236140_at	GCLM	glutamate-cystein...	2730	-0.40927	0.40824	46.539
200651_at	GNB2L1	guanine nucleotid...	10399	-0.26820	0.44107	50.282
222034_at	GNB2L1	guanine nucleotid...	10399	-0.11622	0.27818	31.712
209945_s_at	GSK3B	glycogen synthase...	2932	-0.05020	0.82535	94.090
200824_at	GSTP1	glutathione S-tra...	2950	-0.13805	0.66708	76.047
209960_at	HGF	hepatocyte growth...	3082	-0.16625	0.01933	*
209961_s_at	HGF	hepatocyte growth...	3082	-0.06112	0.24237	27.630
210755_at	HGF	hepatocyte growth...	3082	-0.01139	0.81930	93.400
210997_at	HGF	hepatocyte growth...	3082	-0.01969	0.80248	91.483
210998_s_at	HGF	hepatocyte growth...	3082	0.08873	0.01403	*
200989_at	HIF1A	hypoxia-inducible...	3091	-0.17854	0.32502	37.052
238869_at	HIF1A	hypoxia-inducible...	3091	-0.06248	0.39241	44.735
210211_s_at	HSP90AA1	heat shock protei...	3320	-0.03553	0.89276	101.774
211968_s_at	HSP90AA1	heat shock protei...	3320	-0.17152	0.59731	68.094
211969_at	HSP90AA1	heat shock protei...	3320	0.00820	0.97883	111.586
214328_s_at	HSP90AA1	heat shock protei...	3320	-0.09135	0.62366	71.097
206689_x_at	HTATIP	HIV-1 Tat interac...	10524	0.06400	0.39042	44.508
209192_x_at	HTATIP	HIV-1 Tat interac...	10524	-0.04614	0.49932	56.922
214258_x_at	HTATIP	HIV-1 Tat interac...	10524	0.23690	0.04599	*
201185_at	HTRA1	HtrA serine pepti...	5654	-0.33517	0.48032	54.757
204883_s_at	HUS1	HUS1 checkpoint h...	3364	-0.03670	0.86940	99.111
204884_s_at	HUS1	HUS1 checkpoint h...	3364	-0.03910	0.30805	35.118
217618_x_at	HUS1	HUS1 checkpoint h...	3364	-0.21883	0.26238	29.912
204401_at	KCNN4	potassium interme...	3783	0.30072	0.27106	30.901
209351_at	KRT14	keratin 14 (epide...	3861	-1.01231	0.30247	34.481
205157_s_at	KRT17	keratin 17	3872	-0.41186	0.20121	22.938
212236_x_at	KRT17	keratin 17	3872	-0.49570	0.25852	29.471
201596_x_at	KRT18	keratin 18	3875	0.04396	0.93647	106.757
201820_at	KRT5	keratin 5 (epider...	3852	0.03982	0.93448	106.530
209008_x_at	KRT8	keratin 8	3856	-0.06207	0.59667	68.021
214399_s_at	KRT8	keratin 8	3856	-0.04928	0.32388	36.923
1552263_at	MAPK1	mitogen-activated...	5594	0.10908	0.62605	71.369
1552264_a_at	MAPK1	mitogen-activated...	5594	0.38647	0.01979	*
1562283_at	MAPK1	mitogen-activated...	5594	-0.00740	0.85562	97.540
208351_s_at	MAPK1	mitogen-activated...	5594	0.08651	0.16777	19.126
212271_at	MAPK1	mitogen-activated...	5594	-0.07531	0.73369	83.641
224620_at	MAPK1	mitogen-activated...	5594	-0.06298	0.23773	27.102

224621_at	MAPK1 mitogen-activated...	5594	-0.02757	0.90813	103.526
229847_at	MAPK1 mitogen-activated...	5594	-0.03696	0.54512	62.144
242106_at	MAPK1 mitogen-activated...	5594	-0.00496	0.94046	107.213
202530_at	MAPK14 mitogen-activated...	1432	-0.17572	0.45547	51.923
210449_x_at	MAPK14 mitogen-activated...	1432	0.00852	0.90127	102.745
211087_x_at	MAPK14 mitogen-activated...	1432	0.04245	0.23525	26.818
211561_x_at	MAPK14 mitogen-activated...	1432	-0.03686	0.60280	68.720
232876_at	MAPK14 mitogen-activated...	1432	-0.06228	0.38330	43.696
212046_x_at	MAPK3 mitogen-activated...	5595	0.06503	0.64335	73.342
210477_x_at	MAPK8 mitogen-activated...	5599	-0.09774	0.30549	34.825
210671_x_at	MAPK8 mitogen-activated...	5599	-0.05293	0.49739	56.703
226046_at	MAPK8 mitogen-activated...	5599	-0.02838	0.85832	97.848
226048_at	MAPK8 mitogen-activated...	5599	-0.11115	0.18063	20.592
243280_at	MAPK8 mitogen-activated...	5599	-0.02672	0.72388	82.523
205385_at	MDM2 Mdm2, transformed...	4193	-0.02741	0.50453	57.516
205386_s_at	MDM2 Mdm2, transformed...	4193	0.00283	0.92526	105.480
211832_s_at	MDM2 Mdm2, transformed...	4193	0.00839	0.78303	89.265
217373_x_at	MDM2 Mdm2, transformed...	4193	0.11590	0.26349	30.038
237891_at	MDM2 Mdm2, transformed...	4193	0.00146	0.94761	108.027
204880_at	MGMT 0-6-methylguanine...	4255	0.01252	0.90497	103.167
1567013_at	NFE2L2 nuclear factor (e...	4780	0.01808	0.72616	82.782
1567014_s_at	NFE2L2 nuclear factor (e...	4780	-0.04083	0.35279	40.218
1567015_at	NFE2L2 nuclear factor (e...	4780	0.06915	0.10758	12.264
201146_at	NFE2L2 nuclear factor (e...	4780	-0.32899	0.19910	22.698
239240_at	NFE2L2 nuclear factor (e...	4780	-0.12124	0.43283	49.343
243113_at	NFE2L2 nuclear factor (e...	4780	0.03609	0.23385	26.658
207202_s_at	NR1I2 nuclear receptor ...	8856	0.00776	0.92024	104.907
207203_s_at	NR1I2 nuclear receptor ...	8856	0.12110	0.12343	14.072
240035_at	NR1I2 nuclear receptor ...	8856	0.03346	0.46536	53.052
205301_s_at	OGG1 8-oxoguanine DNA ...	4968	0.05662	0.69690	79.446
205760_s_at	OGG1 8-oxoguanine DNA ...	4968	0.00047	0.99604	113.549
206228_at	PAX2 paired box 2	5076	-0.00344	0.97034	110.619
206229_x_at	PAX2 paired box 2	5076	0.06391	0.27937	31.848
201202_at	PCNA proliferating cel...	5111	0.28441	0.39734	45.297
202545_at	PRKCD protein kinase C,...	5580	0.01468	0.73085	83.317
204053_x_at	PTEN phosphatase and t...	5728	0.12344	0.71998	82.078
204054_at	PTEN phosphatase and t...	5728	-0.10200	0.57708	65.787
211711_s_at	PTEN phosphatase and t...	5728	-0.10816	0.74369	84.781
222176_at	PTEN phosphatase and t...	5728	-0.01558	0.66058	75.306
225363_at	PTEN phosphatase and t...	5728	-0.23356	0.37030	42.214
227469_at	PTEN phosphatase and t...	5728	-0.07355	0.17877	20.380
233254_x_at	PTEN phosphatase and t...	5728	-0.05702	0.50239	57.273
233314_at	PTEN phosphatase and t...	5728	-0.04379	0.31704	36.143
240964_at	PTEN phosphatase and t...	5728	-0.10718	0.04638	*
242622_x_at	PTEN phosphatase and t...	5728	-0.06650	0.03160	*
203132_at	RB1 retinoblastoma 1 ...	5925	-0.07488	0.87784	100.074
211540_s_at	RB1 retinoblastoma 1 ...	5925	0.03937	0.42256	48.172

239169_at	RDM1	RAD52 motif 1	201299	-0.09251	0.22172	25.277
218428_s_at	REV1	REV1 homolog (S. . .)	51455	0.03578	0.92397	105.333
222628_s_at	REV1	REV1 homolog (S. . .)	51455	0.09536	0.29377	33.490
222629_at	REV1	REV1 homolog (S. . .)	51455	0.01080	0.95807	109.220
232236_at	REV1	REV1 homolog (S. . .)	51455	-0.09315	0.13189	15.035
243592_at	REV1	REV1 homolog (S. . .)	51455	-0.03389	0.39954	45.547
201476_s_at	RRM1	ribonucleotide re...	6240	0.00877	0.90914	103.642
201477_s_at	RRM1	ribonucleotide re...	6240	-0.35426	0.37545	42.801
203455_s_at	SAT1	spermidine/spermi...	6303	-0.40537	0.07222	.
210592_s_at	SAT1	spermidine/spermi...	6303	-0.36362	0.18457	21.041
210593_at	SAT1	spermidine/spermi...	6303	0.02375	0.60350	68.799
213988_s_at	SAT1	spermidine/spermi...	6303	-0.34666	0.16197	18.465
230333_at	SAT1	spermidine/spermi...	6303	-0.31859	0.14032	15.996
1555551_at	SERPINB5	serpin peptidase ...	5268	0.00179	0.95219	108.549
204855_at	SERPINB5	serpin peptidase ...	5268	-0.58990	0.34346	39.154
209260_at	SFN	stratifin	2810	0.08379	0.50758	57.865
33322_i_at	SFN	stratifin	2810	0.02906	0.96544	110.060
33323_r_at	SFN	stratifin	2810	0.18229	0.80469	91.734
203971_at	SLC31A1	solute carrier fa...	1317	-0.65114	0.03152	*
235013_at	SLC31A1	solute carrier fa...	1317	-0.12553	0.15112	17.227
236217_at	SLC31A1	solute carrier fa...	1317	-0.01208	0.82663	94.236
209420_s_at	SMPD1	sphingomyelin pho...	6609	-0.20121	0.10744	12.248
216230_x_at	SMPD1	sphingomyelin pho...	6609	0.03017	0.52709	60.089
217171_at	SMPD1	sphingomyelin pho...	6609	-0.02077	0.69253	78.948
1553685_s_at	SP1	Sp1 transcription...	6667	0.06111	0.16673	19.007
214732_at	SP1	Sp1 transcription...	6667	0.01361	0.77765	88.653
224754_at	SP1	Sp1 transcription...	6667	-0.11682	0.48000	54.719
224760_at	SP1	Sp1 transcription...	6667	0.06860	0.46078	52.529
200956_s_at	SSRP1	structure specifi...	6749	-0.08031	0.37085	42.277
200957_s_at	SSRP1	structure specifi...	6749	-0.11291	0.61612	70.238
208991_at	STAT3	signal transducer...	6774	0.11460	0.79239	90.333
208992_s_at	STAT3	signal transducer...	6774	0.32708	0.01853	*
225289_at	STAT3	signal transducer...	6774	0.00407	0.96420	109.919
235680_at	STAT3	signal transducer...	6774	-0.08622	0.08661	.
243213_at	STAT3	signal transducer...	6774	-0.02351	0.71394	81.390
205727_at	TEP1	telomerase-associ...	7011	0.05942	0.16574	18.894
228670_at	TEP1	telomerase-associ...	7011	0.20124	0.18239	20.793
1555271_a_at	TERT	telomerase revers...	7015	0.00241	0.95478	108.844
207199_at	TERT	telomerase revers...	7015	0.01301	0.87249	99.464
202687_s_at	TNFSF10	tumor necrosis fa...	8743	0.29838	0.62204	70.912
202688_at	TNFSF10	tumor necrosis fa...	8743	0.73717	0.14229	16.221
214329_x_at	TNFSF10	tumor necrosis fa...	8743	0.30882	0.64566	73.605
201291_s_at	TOP2A	topoisomerase (DN...	7153	-0.47097	0.33855	38.595
201292_at	TOP2A	topoisomerase (DN...	7153	-0.27728	0.55604	63.388
237469_at	TOP2A	topoisomerase (DN...	7153	-0.05781	0.35206	40.134
1569097_at	TP53BP1	tumor protein p53...	7158	0.00674	0.83659	95.371
1569098_s_at	TP53BP1	tumor protein p53...	7158	0.01415	0.78381	89.354

203050_at	TP53BP1 tumor protein p53...	7158	-0.11300	0.42171	48.075
227907_at	TP53BP1 tumor protein p53...	7158	-0.17500	0.28768	32.795
203120_at	TP53BP2 tumor protein p53...	7159	-0.16809	0.60181	68.607
244536_at	TP53BP2 tumor protein p53...	7159	-0.07465	0.39864	45.445
1555581_a_at	TP63 tumor protein p63	8626	0.00021	0.99675	113.629
207382_at	TP63 tumor protein p63	8626	-0.04908	0.46832	53.388
209863_s_at	TP63 tumor protein p63	8626	-0.13781	0.22400	25.536
211193_at	TP63 tumor protein p63	8626	0.00522	0.93415	106.493
211194_s_at	TP63 tumor protein p63	8626	0.01526	0.80673	91.967
211195_s_at	TP63 tumor protein p63	8626	0.00422	0.91593	104.416
211834_s_at	TP63 tumor protein p63	8626	-0.00335	0.94136	107.315
1554379_a_at	TP73 tumor protein p73	7161	0.11801	0.13076	14.907
220804_s_at	TP73 tumor protein p73	7161	0.04661	0.57040	65.025
232546_at	TP73 tumor protein p73	7161	-0.00289	0.94108	107.283
208864_s_at	TXN thioredoxin	7295	-0.11079	0.68024	77.547
216609_at	TXN thioredoxin	7295	0.09401	0.68387	77.961
202316_x_at	UBE4B ubiquitination fa...	10277	0.09826	0.18971	21.626
202317_s_at	UBE4B ubiquitination fa...	10277	-0.20604	0.35166	40.089
210685_s_at	UBE4B ubiquitination fa...	10277	-0.09579	0.27837	31.734
215533_s_at	UBE4B ubiquitination fa...	10277	0.06134	0.44857	51.137
226746_s_at	UBE4B ubiquitination fa...	10277	0.10112	0.31241	35.615
238414_at	UBE4B ubiquitination fa...	10277	0.03416	0.40127	45.745
238415_at	UBE4B ubiquitination fa...	10277	0.06476	0.38382	43.755
206536_s_at	XIAP X-linked inhibito...	331	-0.00746	0.86718	98.859
206537_at	XIAP X-linked inhibito...	331	-0.09692	0.28867	32.909
225858_s_at	XIAP X-linked inhibito...	331	-0.18625	0.45705	52.103
225859_at	XIAP X-linked inhibito...	331	-0.09972	0.54504	62.134
228363_at	XIAP X-linked inhibito...	331	-0.07588	0.82649	94.220
235222_x_at	XIAP X-linked inhibito...	331	-0.26763	0.11125	12.683
243026_x_at	XIAP X-linked inhibito...	331	-0.11029	0.03594	*
209375_at	XPC xeroderma pigment...	7508	0.08064	0.60624	69.111
213342_at	YAP1 Yes-associated pr...	10413	0.12994	0.74855	85.335
224894_at	YAP1 Yes-associated pr...	10413	-0.22518	0.63293	72.154
224895_at	YAP1 Yes-associated pr...	10413	0.09990	0.70626	80.514
208627_s_at	YBX1 Y box binding pro...	4904	-0.32164	0.30631	34.920
208628_s_at	YBX1 Y box binding pro...	4904	-0.20576	0.50926	58.056

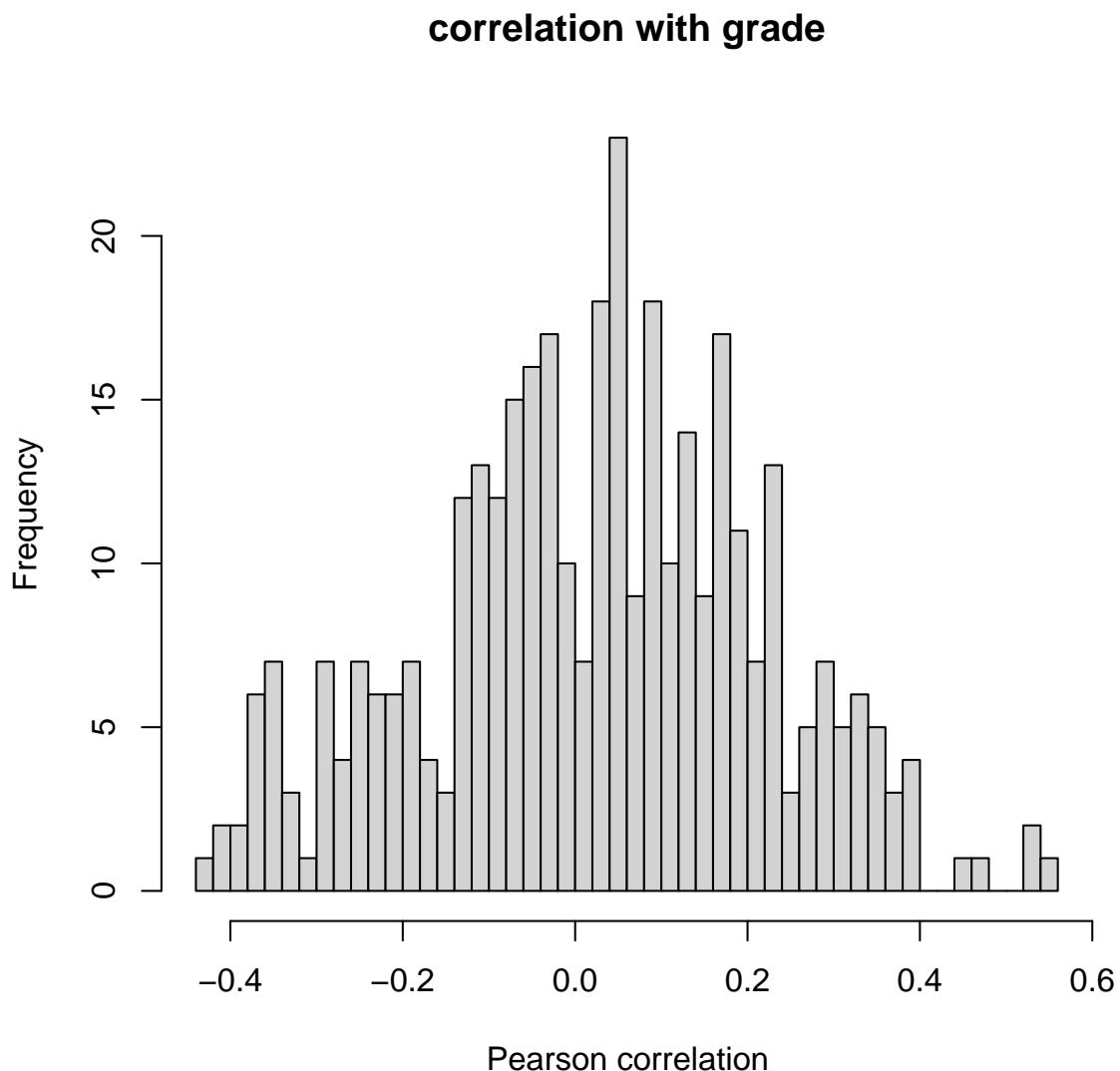
> options(width = 70)

3 Evaluation of genes by correlation to grade

3.1 Calculate correlations for each gene

```
> corr <- cor(t(exprs(plat.rma.sub)), grade)[, 1]
> corr.p <- apply(exprs(plat.rma.sub), 1, function(x) cor.test(x,
+     grade)$p.value)

> hist(corr, n = 40, col = "lightgray", xlab = "Pearson correlation",
+     main = "correlation with grade")
```



3.2 List the most highly-correlated probe sets

```
> d2 <- cbind(d[, 1:3], corr = corr, p.val = corr.p, corrected = corr.p *
+      nh)
> interesting <- abs(d2$corr) > 0.4
> print(d2[interesting, ][order(d2$corr[interesting])],
+      ], digits = 2)
```

	symbol	gene	entrez	corr	p.val	corrected
210998_s_at	HGF hepatocyte growth...	3082	-0.44	0.0325		3.70
206155_at	ABCC2 ATP-binding casse...	1244	-0.41	0.0466		5.31
209835_x_at	CD44 CD44 molecule (In...	960	-0.41	0.0479		5.46
1560395_at	CD24	934	0.44	0.0314		3.58
1562028_at	CCND3	896	0.47	0.0217		2.48
202095_s_at	BIRC5 baculoviral IAP r...	332	0.52	0.0087		0.99
210334_x_at	BIRC5 baculoviral IAP r...	332	0.54	0.0066		0.75
243353_at	AIFM1 apoptosis-inducin...	9131	0.56	0.0047		0.53

4 sessionInfo

The results in this file are generated using the following packages:

```
> sessionInfo()

R version 2.7.1 (2008-06-23)
ia64-unknown-linux-gnu

locale:
LC_CTYPE=en_US.UTF-8;LC_NUMERIC=C;LC_TIME=en_US.UTF-8;LC_COLLATE=en_US.UTF-8;LC_MONETARY=C

attached base packages:
[1] splines   tools     stats      graphics  grDevices utils
[7] datasets  methods   base

other attached packages:
[1] hgu133plus2.db_2.2.0 AnnotationDbi_1.2.2  RSQLite_0.6-9
[4] DBI_0.2-4           genefilter_1.20.1  survival_2.34-1
[7] gdata_2.4.2         affy_1.18.2       preprocessCore_1.2.0
[10] affyio_1.8.0        Biobase_2.0.1

loaded via a namespace (and not attached):
[1] annotate_1.18.0 gtools_2.5.0

> system("uname -a", intern = TRUE)

[1] "Linux sbiology 2.6.16.46-0.12-default #1 SMP Thu May 17 14:00:09 UTC 2007 ia64 ia64 i"
```